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Analysis of the radiological detriment for premenopausal women in a breast early detection program during 2008

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Abstract— **The Valencian Breast Cancer Early Detection Program (VBCEDP) started in the Valencian Community (Spain) in 1992. Up to now, 24 mammographic units have been installed all over the region. Mammography is used to aid in the diagnosis of breast cancer diseases in women. There is a health risk in the studied women due to ionising radiation that has to be estimated and controlled. A methodology to calculate approximately the radiological detriment in the VBCEDP has been developed based on Monte Carlo techniques. It has been used, as qualitative parameter, the average mean glandular dose from representative sample populations undergoing screening mammography (digital or screenfilm) from each of the twenty-four units in operation. The American College of Radiology Imaging Network reached to conclusion that digital mammography performed significantly better than film for pre and perimenopausal women younger than 50. Women who are undergoing the program are between 45 and 69. This fact allows us to study premenopausic women. Our group uses the software SCREENRISK to estimate induction and mortality rates in order to corroborate American conclusions in an European region. The obtained results confirm the American results about the application of digital mammography in pre and perimenopausal women younger than 50 years.**

I. Introduction

SCREENING mammographic programs try to get an early diagnosis of the breast cancer in middle aged women. The European Protocol on Dosimetry in Mammography [3] is the document that regulates this practice, allowing quality on the diagnostic and the comparison between differents screening units.

Although screening for the early detection of breast diseases reduces breast cancer mortality, it is well known that the diagnosis by mammography presents risks for women undergoing screening due to the exposition to ionising radiation. At present, it is considered the mean glandular dose (MGD) in acquiring the mammography as a risk parameter. Then it is possible to use the MGD in order to obtain the risk of induced breast cancers in a screening programme. Risk projection models obtained from data of exposed populations, such as the survivors of the atomic bombs or patients exposed to high doses due to medical reasons have been used.

It is important to to remember that Life Span Study could have a possible contribution of neutrons in the radiological risk. Mammography uses photons of 32 keV so neutron influence on detriment is improbable. It must be taken into consideration that there are very few population models in order to study incidence and mortality cancers

This way of proceeding has many uncertainties but these indicators are right to compare how mammographic units act on different phases in a prevention program. That was the reason of the development of SCREENRISK. This software based on Matlab© gives us an easy way of quantifying risks in mammographic screening programs.

II. Methodology

A. Excess relative risk for incidence and mortality

The excess relative risk (ERR) is a parameter used to transport risks between populations which have been exposed to radiation and have different baseline rates. Risk projection models are used in epimediology in order to estimate incidence and mortality cancer rates in one population under study from data that has been obtained in other populations.

Different studies have been chosen to estimate risks in the Valencian Breast Cancer Early Detection Program. The mortality models are: (1a) Life Span Study cohort (LSS) that includes female bomb survivors between 1950 and 1985; (2a) and the LSS with follow-up until 1990 depending on age at exposure and (3a) depending on attained age. The incidence models for breast cancer are: (1b) the Life Span Study for incidence breast cancer (1958-1993); (2b) the Massachussets fluoroscopy study, for tuberculosis patients (TBO) and the extension (TBX); (3b) the New York acute post-partum mastitis cohort (APM); and (4b) the bening breast disease treatment in Sweden (BBD).

The excess relative risk is fitted with

$$ERR\left(\vec{z}^{(m)}\right) = \alpha^{(m)}\theta(s)\Phi(\vec{D}_g)\exp\left[\gamma^{(m)}(t_e - t^{(m)})\right]\left(\frac{t_k}{50}\right)^{\beta^{(m)}} \quad (1)$$

thus $\Phi(D_g)$ is the dose response with dose D_g to the breast, s is the gender of the individual and $\theta(s)$ is a function that depends on gender and cancer type, equal to unity for breast cancer on female. The covariate vector for the ERR is the

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same for incidence and mortality, and it includes the variables. Each model has its own parameters based on cases under study.

In order to transport the risks, there has been applied an extension of Cox Proportional Hazards to estimate the Excess Absolute Risk (EAR) as

$$EAR^{(m)}(t_k \mid \vec{z}^{(m)}) = \lambda(t_k)\left[ERR(\vec{z}^{(m)})\right] \qquad (2)$$
$$t_k \geq t_e + L$$

therefore ERR (z^m) is the excess relative risk of the model m for breast cancer. In (2), it is observed that ERR(z^m) is transported to a population with a risk base function λ(tk) for incidence or mortality.

B. Risk of exposure-induced cancer (REIC) and death (REID)

The risk of exposure induced cancer (REIC) is defined as the probability of an individual develops a radio-induced cancer, not necessarily mortal, all over his life. The risk of exposure induced death (REID) shows the probability that an individual dies due to a radio-induced cancer. So, deriving a Markov process, REIC and REID can be obtained as

$$REID\ (t_e \mid \vec{z}_{fbc}) = \sum_{j=e+L}^{M} \hat{s}_1(t_j \mid \vec{z}_{fbc}) EAR_{fbc}(t_j \mid \vec{z}_{fbc}) \quad (3)$$

$$REIC\ (t_e \mid \vec{z}_{in}, \vec{z}_{fbc}) = \sum_{j=e+L}^{M} \hat{s}_1(t_j \mid \vec{z}_{fbc}) EAR_{in}(t_j \mid \vec{z}_{in}) \quad (4)$$

thus the estimator of the survival function, EAR_{fbc} is the excess absolute risk for mortal breast cancer and EAR_{in} for incidence. $\vec{z}_{in}$ is the vector of covariates for breast cancer incidence.

C. The SCREENRISK software: simulation and implementation

In a breast screening program, women are invited to undergo mammography between an initial age (*a*) and a final age (*b*), with a constant screen interval (*s*) and receiving normally one exposure per breast at each time.

There are different indicators when evaluating the associated cancer risk during breast screening. These indicators are adequate to make comparisons between several programs. One of these is the average radiological detriment for breast cancer incidence and mortality, in a given instant of the screening and can be estimated as

$$\Pi_{in}^{(m)} = \sum_{j=a}^{b} \nu(t_j) REIC^{(m)}(t_j \mid \overrightarrow{d_{gj}}) \cdot \omega(t_j) \qquad (5)$$

$$\Pi_{fbc}^{(m)} = \sum_{j=a}^{b} \nu(t_j) REID^{(m)}(t_j \mid \overrightarrow{d_{gj}}) \cdot \omega(t_j) \qquad (6)$$

where $v\ (t_j)$ is the number of views per breast in each visit, $\omega\ (t_j)$ is the fraction of population and d_{gj} is the average mean glandular dose per film at an age-at-exposure t_j.

Using this methodology, some of the authors (M. Ramos and G.Verdu) developed SCREENRISK software in 2005 [2.]. It is based on *Matlab© 6.5* which estimates the risk of exposure-induced cancer and fatal cancer for a specific cancer in a given population.

D. The Valencian Breast Early Detection Program and the digital mammography.

The Valencian Breast Cancer Early Detection Program started in 1992 and actually 24 units are working on that. Yearly quality controls are performed in all units with the recommendations of the European Protocol on Dosimetry in Mammography

The VBCEDP is directed towards asymptomatic women between 45 and 69 years old, with an initial age lower than other screening programs (i.e. UK Screening Program starts at the age of 50 years). The screening examination consists of two exposures per breast; craniocaudal (CC) and mediolateral oblique (OBL). The first time that the woman participates in the program (first round) receives two exposures per breast and a single mammogram OBL per breast in subsequent rounds. The screening rounds are spaced every two years and two independent radiologists read each mammogram.

Each six months population samples are taken from the screening units involved in the program in order to estimate and control the radiological risk.

In this work, it has been analyzed the radiological detriment of premenopausal or perimenopausal women under 50 years and postmenopausal women who participated in the Valencian screening program comparing those screened with a digital mammography versus screen-film mammography.

III. RESULTS

The results have been calculated for the first and second semester of 2008. A sample of 900 women was considered for the first semester and 1200 for the second one who followed the screening program.

Table I shows the induced cancers calculated using SCREENRISK software where premenopausal and postmenopausal women are compared for each incidence model. The values are presented as number of induced cancers per 100000 women. In the same way, results of fatal induced cancers per 10^5 women are showed in Table II. These tables correspond to the first-semester sample of 2008. (Digital mammography is represented in the tables as DM)

TABLE I
INDUCED CANCERS PER 10^5 WOMEN FIRST SEMESTER 2008

Models	Premenopausic		Postmenopausic	
	Screenfilm	DM	Screenfilm	DM
LSS Attained age	5.97 ± 3.94	5.59 ± 1.07	6.84 ± 5.22	6.58 ± 3.46
TBO Attained age	2.10 ± 1.39	1.97 ± 0.38	2.41 ± 1.84	2.32 ± 1.22
APM All ages	3.09 ± 1.98	2.85 ± 0.54	3.73 ± 2.91	3.67 ± 1.95
BBD Exposition age	1.07 ± 0.78	1.06 ± 0.19	1.01 ± 0.67	0.85 ± 0.43

TABLE II
FATAL INDUCED CANCERS PER 10^5 WOMEN FIRST SEMESTER 2008

Models	Premenopausic		Postmenopausic	
	Screenfilm	DM	Screenfilm	DM
LSS (1950-1985) Exposition age	0.85 ± 0.56	0.82 ± 1.16	0.89 ± 0.65	0.82 ± 0.42
LSS (1950-1990) Exposition age	1.68 ± 1.15	1.61 ± 0.31	1.79 ± 1.31	1.66 ± 0.86
LSS (1950-1990) Attained age	3.92 ± 2.56	3.66 ± 0.69	4.55 ± 3.49	4.40 ± 2.32

Table III shows the induced cancers calculated using SCREENRISK software where premenopausal and postmenopausal women are compared for each incidence model. The values are presented as number of induced cancers per 100000 women. In the same way, results of fatal induced cancers per 10^5 women are showed in Table IV. These tables correspond to the second-semester sample of 2008.

TABLE III
INDUCED CANCERS PER 10^5 WOMEN SECOND SEMESTER 2008

	Premenopausic		Postmenopausic	
	Screenfilm	DM	Screenfilm	DM
LSS Attained age	5.13 ± 3.79	4.03 ± 1.83	6.04 ± 3.08	6.31 ± 3.34
TBO Attained age	1.81 ± 1.34	1.42 ± 0.64	2.13 ± 1.08	2.22 ± 1.18
APM All ages	2.63 ± 1.90	2.02 ± 0.91	3.29 ± 1.71	3.43 ± 1.84
BBD Exposition age	0.94 ± 0.76	0.79 ± 0.36	0.88 ± 0.41	0.95 ± 0.47

TABLE IV
FATAL INDUCED CANCERS PER 10^5 WOMEN SECOND SEMESTER 2008

Models	Premenopausic		Postmenopausic	
	Screenfilm	DM	Screenfilm	DM
LSS (1950-1985) Exposition age	0.74 ± 0.57	0.60 ± 0.27	0.78 ± 0.39	0.83 ± 0.43
LSS (1950-1990) Exposition age	1.46 ± 1.11	1.17 ± 0.53	1.58 ± 0.78	1.66 ± 0.86
LSS (1950-1990) Attained age	3.35 ± 2.47	2.62 ± 1.19	4.02 ± 2.06	4.19 ± 2.23

IV. CONCLUSION

SCREENRISK provides an easy and fast way of calculating the radiological detriment in medical expositions due to ionising radiation, such as the Valencian Breast Screening Program. The obtained results for the VBCEDP shows a lower detriment in premenopausal women screened using digital mammography in front of screen-film mammography. It is also appreciated that the detriment in postmenopausal women is higher than premenopausic using digital mammography except for the value of the first semester using BBD model. This fact could be due to the higher uncertainties that models carry with.

According to the results, it is observed that the differences in detriment between premenopausal and postmenopausal women are not constant among models. It is difficult to reach to conclusion about it because population models concerning to fatal breast cancer due to radiation exposure are subjected to multiple uncertainties.

These results corroborate the work of Pisano et al. [1] but it is also recommended to increase the volume of screened women in order to achieve more confident values.

In spite of this, risk transport from any model is a good indicator to compare different screening units and programs.

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